AMENDMENTS TO THE CLAIMS

1. (currently amended) A chimeric protein comprising:

(a) a Kunitz-type domain 1 of Tissue Factor Pathway Inhibitor-2 (TFPI-2) ~~TFPI-2~~ or a mutein thereof, wherein the mutein is selected from the group consisting of:

(i) a Kunitz-type domain 1 of TFPI-2 comprising 1-5 conservative amino acid substitutions that do not substantially change the conformation of TFPI-2;

(ii) a Kunitz-type domain 1 of TFPI-2 comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 1 of TFPI-2 which has 1-5 amino acid substitutions that change a residue of TFPI-2 to a corresponding residue of TFPI; and

(iv) a Kunitz-type domain 1 of TFPI-2 that comprises an amino acid substitution in the P_1 reactive site and

(b) a Kunitz-type domain 2 of Tissue Factor Pathway Inhibitor (TFPI) ~~TFPI~~ or a mutein thereof, wherein the mutein is selected from the group consisting of:

(i) a Kunitz-type domain 2 of TFPI comprising 1-5 conservative amino acid substitutions that do not substantially change the conformation of TFPI-2;

(ii) a Kunitz-type domain 2 of TFPI comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 2 of TFPI which has 1-5 amino acid substitutions that change a residue of TFPI to a corresponding residue of TFPI-2; and

(iv) a Kunitz-type domain 2 of TFPI that comprises an amino acid substitution in the P_1 reactive site; or

(c) a Kunitz-type domain 2 of TFPI-2 or a mutein thereof, wherein the mutein is selected from the group consisting of:

(i) a Kunitz-type domain 2 of TFPI-2 comprising 1-5 conservative amino acid substitutions that do not substantially change the conformation of TFPI-2;

(ii) a Kunitz-type domain 2 of TFPI-2 comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 2 of TFPI-2 which has 1-5 amino acid substitutions that change a residue of TFPI-2 to a corresponding residue of TFPI; and

(iv) a Kunitz-type domain 2 of TFPI-2 that comprises an amino acid substitution in the P_1 reactive site; and

(d) a Kunitz-type domain 1 of TFPI or a mutein thereof, wherein the mutein is selected from the group consisting of:

(i) a Kunitz-type domain 1 of TFPI comprising 1-5 conservative amino acid substitutions that do not substantially change the conformation of TFPI;

(ii) a Kunitz-type domain 1 of TFPI comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 1 of TFPI which has 1-5 amino acid substitutions that change a residue of TFPI to a corresponding residue of TFPI-2; and

(iv) a Kunitz-type domain 1 of TFPI that comprises an amino acid substitution in the P_1 reactive site,

wherein the chimeric protein binds and inhibits factor VIIa / tissue factor complex and binds to and inhibits factor Xa.

2. (currently amended) The chimeric protein of claim 1, wherein said chimeric protein is represented by the generic structure:

$$A\text{-}(X_1)_a\text{-}B\text{-}(X_2)_b\text{-}C$$

wherein A and C are independently optional flanking peptides, the flanking peptides containing 0-100 amino acids;

wherein B is an optional spacer peptide, the spacer peptide containing 0-25 amino acids;

wherein each X_1 is -D-K_1-E-

where D, E are independently peptides of 0-25 amino acids,

where K_1 comprises TFPI Kunitz-type domain 1 or a mutein thereof or TFPI-2 Kunitz-type domain 1 or a mutein thereof, wherein the mutein of the TFPI Kunitz-type domain 1 is selected from the group consisting of:

(i) a Kunitz-type domain 1 of TFPI comprising 1-5 conservative amino acid substitutions that do no substantially change the conformation of TFPI;

(ii) a Kunitz-type domain 1 of TFPI comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 1 of TFPI which has 1-5 amino acid substitutions that change a residue of TFPI to a corresponding residue of TFPI-2; and

(iv) a Kunitz-type domain 1 of TFPI that comprises an amino acid substitution in the P_1 reactive site,

and wherein the mutein of TFPI-2 Kunitz-type domain 1 is selected from the group consisting of:

(i) a Kunitz-type domain 1 of TFPI-2 comprising 1-5 conservative amino acid substitutions that do not substantially change the conformation of TFPI-2;

(ii) a Kunitz-type domain 1 of TFPI-2 comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 1 of TFPI-2 which has 1-5 amino acid substitutions that change a residue of TFPI-2 to a corresponding residue of TFPI; and

(iv) a Kunitz-type domain 1 of TFPI-2 that comprises an amino acid substitution in the P_1 reactive site,

wherein each X_2 is -F-K_2-G-

where F, G are independently peptides of 0-25 amino acids,

where K_2 comprises TFPI Kunitz-type domain 2 or a mutein thereof or TFPI-2 Kunitz-type domain 2 or a mutein thereof, wherein the mutein of TFPI Kunitz-type domain 2 is selected from the group consisting of:

(i) a Kunitz-type domain 2 of TFPI comprising 1-5 conservative amino acid substitutions that do not substantially change the conformation of TFPI-2;

(ii) a Kunitz-type domain 2 of TFPI comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 2 of TFPI which has 1-5 amino acid substitutions that change a residue of TFPI to a corresponding residue of TFPI-2; and

(iv) a Kunitz-type domain 2 of TFPI that comprises an amino acid substitution in the P_1 reactive site,

and wherein the mutein of TFPI-2 Kunitz-type domain 2 is selected from the group consisting of:

(i) a Kunitz-type domain 2 of TFPI-2 comprising 1-5 conservative amino acid substitutions that do not substantially change the conformation of TFPI-2;

(ii) a Kunitz-type domain 2 of TFPI-2 comprising an amino acid substitution that eliminates an N-linked glycosylation site;

(iii) a Kunitz-type domain 2 of TFPI-2 which has 1-5 amino acid substitutions that change a residue of TFPI-2 to a corresponding residue of TFPI; and

(iv) a Kunitz-type domain 2 of TFPI-2 that comprises an amino acid substitution in the P_1 reactive site,

wherein a, b are integers from 1-6; and

the chimeric protein is not native TFPI or TFPI-2.

3. (original) The chimeric protein of claim 2, wherein A or C comprises Kunitz-type domain 3 of TFPI.

4. (original) The chimeric protein of claim 2, wherein A or C comprises Kunitz-type domain 3 of TFPI-2.

5. (original) The chimeric protein of claim 2, wherein at least one of said flanking peptides comprises an amino acid sequence capable of binding one or more cell surface components.

6. (original) The chimeric protein of claim 5, wherein said amino acid sequence capable of binding one more cell surface components is an amino acid sequence capable of binding a glycosaminoglycan.

7. (original) The chimeric protein of claim 6, wherein said amino acid sequence capable of binding a glycosaminoglycan is an amino acid sequence capable of binding heparin.

8. (original) The chimeric protein of claim 7, wherein said amino acid sequence capable of binding heparin is a heparin-binding domain from a protein, said protein selected from the group consisting of:

(a) protease nexin-1;

(b) protease nexin-2;

(c) antithrombin III;

(d) heparin cofactor II;

(e) protein C inhibitor;

(f) platelet factor 4;

(g) bovine pancreatic trypsin inhibitor; and

(h) ghilanten-related inhibitors.

9. (original) The chimeric protein of claim 7, wherein said amino acid sequence capable of binding heparin is a heparin-binding domain selected from the group consisting of:

(a) SEQ ID NO: 10;

(b) SEQ ID NO: 11;

(c) SEQ ID NO: 12;

(d) SEQ ID NO: 13;

(e) SEQ ID NO: 14;

(f) SEQ ID NO: 15;

(g) SEQ ID NO: 16;

(h) SEQ ID NO: 17; and

(i) SEQ ID NO: 18.

10. (original) The chimeric protein of claim 5, wherein said flanking peptide comprises the C-terminal tail of TFPI [SEQ ID NO: 7].

11. (original) The chimeric protein of claim 5, wherein said flanking peptide comprises the C-terminal tail of TFPI-2 [SEQ ID NO: 8].

12. (canceled)

13. (previously amended) The chimeric protein of claim 2, wherein each K_1 is mutein of Kunitz-type domain 1 of TFPI-2, and each K_2 is a mutein of Kunitz-type domain 2 of TFPI.

14. (previously amended) A chimeric protein, wherein the primary amino acid sequence of the chimeric protein is SEQ ID NO: 19.

15. (previously amended) The chimeric protein of claim 14, wherein the chimeric protein comprises first and second amino acid sequences, said first amino acid sequence comprising SEQ ID NO:19 and said second amino acid sequence selected from the group consisting of:

(a) SEQ ID NO: 7;

(b) SEQ ID NO: 8;

(c) SEQ ID NO: 10;

(d) SEQ ID NO: 11;

(e) SEQ ID NO: 12;

(f) SEQ ID NO: 13;

(g) SEQ ID NO: 14;

(h) SEQ ID NO: 15;

(i) SEQ ID NO: 16;

(j) SEQ ID NO: 17; and

(k) SEQ ID NO: 18.

16. (previously amended) The chimeric protein of claim 1, wherein said chimeric protein is represented by the generic structure:

$$A\text{-}(X_1\text{-}B\text{-}X_2)_c\text{-}C$$

wherein A and C are independently optional flanking peptides, the flanking peptides containing 1-100 amino acids;

wherein B is an optional spacer peptide, the spacer peptide containing 1-25 amino acids;

wherein each X_1 is -D-K_1-E-

where D, E are independently peptides of 1-25 amino acids,

where K_1 is (a) the Kunitz-type domain 1 of TFPI-2 or the mutein thereof or (b) the TFPI Kunitz-type domain 1 of TFPI or the mutein thereof;

wherein each X_2 is -F-K_2-G-

where F, G are independently peptides of 1-25 amino acids,

where K_2 is (a) the Kunitz-type domain 2 of TFPI or the mutein thereof or (b) the Kunitz-type domain 2 of TFPI-2 or the mutein thereof,

wherein c is an integer from 1-10.

17. (original) The chimeric protein of claim 16, wherein A or C comprises Kunitz-type domain 3 of TFPI [SEQ ID NO: 7].

18. (original) The chimeric protein of claim 16, wherein A or C comprises Kunitz-type domain 3 of TFPI-2 [SEQ ID NO: 8].

19. (original) The chimeric protein of claim 16, wherein at least one of said flanking peptides comprises an amino acid sequence capable of binding one or more cell surface components.

20. (original) The chimeric protein of claim 19, wherein said amino acid sequence capable of binding one or more cell surface components is an amino acid sequence that binds glycosaminoglycan.

21. (original) The chimeric protein of claim 20, wherein said amino acid sequence capable of binding glycosaminoglycan is an amino acid sequence capable of binding heparin.

22. (original) The chimeric protein of claim 21, wherein said amino acid sequence capable of binding heparin is a heparin-binding domain from a protein, said protein selected from the group consisting of:

(a) protease nexin-1;

(b) protease nexin-2;

(c) antithrombin III;

(d) heparin cofactor II;

(e) protein C inhibitor;

(f) platelet factor 4;

(g) bovine pancreatic trypsin inhibitor; and

(h) ghilanten-related inhibitors.

23. (original) The chimeric protein of claim 21, wherein said amino acid sequence capable of binding heparin is a heparin-binding domain selected from the group consisting of:

(a) SEQ ID NO: 10;

(b) SEQ ID NO: 11;

(c) SEQ ID NO: 12;

(d) SEQ ID NO: 13;

(e) SEQ ID NO: 14;

(f) SEQ ID NO: 15;

(g) SEQ ID NO: 16;

(h) SEQ ID NO: 17; and

(i) SEQ ID NO: 18.

24. (original) The chimeric protein of claim 19, wherein said flanking peptide comprises the C-terminal tail of TFPI [SEQ ID NO: 7].

25. (original) The chimeric protein of claim 19, wherein said flanking peptide comprises the C-terminal tail of TFPI-2 [SEQ ID NO: 8].

26. (original) The chimeric protein of claim 1 wherein said protein is produced in a yeast cell and contains no carbohydrate which is immunogenic in mammals.

27. (original) The chimeric protein of claim 26 wherein said protein contains no α-1,6-polymannose terminal carbohydrate.

28-72. (canceled)

73. (original) A pharmaceutical composition comprising the chimeric protein of claim 1 and a pharmaceutically acceptable carrier.

74-87. (canceled)

88. (previously added) The chimeric protein of claim 2 wherein each K_1 is a mutein of Kunitz-type domain 1 of TFPI and each K_2 is a mutein of Kunitz-type domain 2 of TFPI-2.

89. (newly added) The chimeric protein of claim 1 wherein the chimeric protein comprises a mutein of the Kunitz-type domain 1 of TFPI that comprises an amino acid substitution in the P_1 reactive site and wherein the amino acid in the P_1 position is arginine.

90. (newly added) The chimeric protein of claim 1 which comprises a mutein of the Kunitz domain 1 of TFPI-2 and a mutein of the Kunitz domain 2 of TFPI and is truncated at the end of the Kunitz domain 2 of TFPI.

91. (newly added) The chimeric protein of claim 1 which comprises a mutein of the Kunitz domain 1 of TFPI-2 and a mutein of the Kunitz domain 2 of TFPI and which does not comprise Kunitz domain 3 of TFPI but does comprise the C-terminal tail of TFPI.

92. (newly added) The chimeric protein of claim 1 which comprises a mutein of the Kunitz domain 2 of TFPI-2 and a mutein of the Kunitz domain 1 of TFPI and is truncated at the end of the Kunitz domain 2 of TFPI-2.

93. (newly added) The chimeric protein of claim 1 which comprises a mutein of the Kunitz domain 2 of TFPI-2 and a mutein of the Kunitz domain 1 of TFPI and does not comprise Kunitz domain 3 of TFPI-2 but does comprise the C-terminal tail of TFPI-2.

94. (newly added) The chimeric protein of claim 2 wherein the chimeric protein comprises a mutein of the Kunitz-type domain 1 of TFPI that comprises an amino acid substitution in the P_1 reactive site and wherein the amino acid in the P_1 position is arginine.

95. (newly added) The chimeric protein of claim 2 which comprises a mutein of the Kunitz domain 1 of TFPI-2 and a mutein of the Kunitz domain 2 of TFPI and is truncated at the end of the Kunitz domain 2 of TFPI.

96. (newly added) The chimeric protein of claim 2 which comprises a mutein of the Kunitz domain 1 of TFPI-2 and a mutein of the Kunitz domain 2 of TFPI and which does not comprise Kunitz domain 3 of TFPI but does comprise the C-terminal tail of TFPI.

97. (newly added) The chimeric protein of claim 2 wherein K_2 comprises a mutein of the Kunitz domain 2 of TFPI-2 and wherein K_1 comprises a mutein of the Kunitz domain 1 of TFPI, wherein the chimeric protein is truncated at the end of the mutein of the Kunitz domain 2 of TFPI-2.

98. (newly added) The chimeric protein of claim 2 wherein K_2 comprises a mutein of the Kunitz domain 2 of TFPI-2 and wherein K_1 comprises a mutein of the Kunitz domain 1 of TFPI, wherein the chimeric protein does not comprise Kunitz domain 3 of TFPI-2 but does comprise the C-terminal tail of TFPI-2.